Application Serial No.: 09/897,107
Response to Office Action of August 26, 2003

AMENDMENTS TO THE CLAIMS

- 1. 16. (Canceled)
- 17. (Currently Amended) A method for improving thermostability of proteins, which comprises:
- (i) comparing amino acid sequences of proteins belonging to the same family that are similar to each other in at least one of the features selected from the group consisting of function, amino acid sequence, domain structure and steric structure and deriving from two or more species, wherein said proteins evolutionarily correspond to each other in a phylogenetic tree which can be obtained by using the maximum parsimony method or the maximal likelihood method and said proteins include proteins from the species selected from the group consisting of thermophilic bacteria and archaebacteria;
- (ii) estimating an amino acid sequence of an ancestral protein corresponding to the amino acid sequences of the proteins in (i), said ancestral protein being located at the root of the phylogenetic tree;
- (iii) comparing the amino acid residues in the amino acid sequence in one of the proteins compared in (i) with amino acid residues at a corresponding position in the ancestral protein estimated in (ii), and replacing one or more amino acid residues of the protein which are different from those of the ancestral protein with the same amino acid residues as those of present in the ancestral protein;
 - (iv) testing the proteins obtained in (iii) for thermostability; and
 - (v) selecting a protein having improved thermostability.
 - 18. (Canceled)
- 19. (Previously Presented) The method of claim 17, wherein the protein being tested for improved thermostability is a 3-isopropylmalate dehydrogenase.

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20. (Previously Presented) The method of claim 17, wherein the protein being tested for improved thermostability is an isocitrate dehydrogenase.

- 21. 22. (Canceled)
- 23. (Currently Amended) A method for improving thermostability of proteins, which comprises
- (i) comparing amino acid sequences of proteins belonging to the same family that are similar to each other in at least one of the features selected from the group consisting of function, amino acid sequence, domain structure and steric structure and deriving from two or more species, wherein said proteins evolutionarily correspond to each other in a phylogenetic tree by multiple alignment, said phylogenetic tree being capable of being obtained by using the maximum parsimony method or the maximal likelihood method and said proteins including proteins from the species selected from the group consisting of thermophilic bacteria and archaebacteria;
- (ii) estimating an amino acid sequence of an ancestral protein corresponding to the amino acid sequences of the proteins in (i), said ancestral protein being located at the root of the phylogenetic tree;
- (iii) comparing the amino acid residues in the amino acid sequence in one of the proteins compared in (i) with amino acid residues at a corresponding position in the ancestral protein estimated in (ii), and replacing one or more amino acid residues of the protein-which are different from those of the ancestral protein with the same amino acid residues as those of present in the ancestral protein;
 - (iv) testing the proteins obtained in (iii) for thermostability; and
 - (v) selecting a protein having improved thermostability.
 - 24. 26. (Canceled)

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- 27. (New) The method of claim 23, wherein the protein being tested for improved thermostability is a 3-isopropylmalate dehydrogenase.
- 28. (New) The method of claim 23, wherein the protein being tested for improved thermostability is an isocitrate dehydrogenase.

SUPPORT FOR THE AMENDMENT

Claims 1-16 were previously canceled.

Claims 18, 21, 22, and 24-26 have been cancelled in the present amendent.

Claims 17 and 23 have been added.

The amendment of Claims 17 and 23 is supported by Claims 1-16 as originally filed.

The specification has also been amended to insert proper sequence identifiers. Support for these amendments can be found in the specification and drawings as originally filed.

No new matter is believed to have been entered by the present amendment.